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Commentary

Bone metastases of prostate cancer: PSMA PET versus bone scan

Ismet Sarikaya, MD, ABNM[1]

[1]Department of Nuclear Medicine, Faculty of Medicine, Kirklareli University, Kırklareli, Turkey

Due to high blood flow in the red bone marrow, bone is a common site of metastasis for various cancers including prostate cancer. Multiple factors and expression of certain genes contribute to the homing of tumor cells to the bone marrow/bone.[1] Tumor cells escape from the circulation into the bone marrow, interact with resident bone marrow cells for survival, and resident bone cells are activated (crosstalk between tumor cells and resident bone and bone marrow cells), which leads to tumor growth in bone.[2] Bone metastases of prostate cancer are osteoblastic (osteosclerotic) in nature. In osteoblastic metastases, there is formation of new bone that is immature and of poor quality. Tumor cells secrete various factors that induce osteoblastic proliferation and differentiation, such as growth factors (TGF-b, VEGF, and FGF).[3] In prostate cancer, prostate-specific antigen and other substances also contribute to modifying the bone microenvironment.

Radionuclide bone imaging (bone scan) is a common procedure in detecting osteoblastic metastases.[4] Bone scan detects bone metastases indirectly by binding to new bone formation among tumor foci in metastatic niche. Compared to traditional diphosphonate bone scan (scintigraphy), 18F-sodium fluoride (NaF) PET bone scan has higher sensitivity in detecting bone metastases.[5] PET can detect small foci, which are below the resolution of gamma cameras. One of the limitations of bone scan is that certain benign lesions such as osteophytes, facet arthritis, and degenerative disk disease can also show increased radiotracer uptake, which may mimic metastases.[6] However, CT component of hybrid PET and gamma cameras (SPECT/CT and PET/CT) is very helpful in differentiating benign from malignant uptake in most of the cases.

A PSA cutoff value of ≥10–20 is recommended for ordering diphosphonate bone scan in newly diagnosed and untreated asymptomatic prostate cancer patients.[7,8] In our original study, we found a PSA cutoff value of >20 ng/mL for ordering NaF PET bone scan in newly diagnosed prostate cancer patients.[9] Recent studies have demonstrated that prostate-specific membrane antigen (PSMA) PET imaging is superior to bone scan in detecting bone metastases of prostate cancer.[10,11] PSMA is a type II transmembrane protein with enzymatic activity (glutamate carboxypeptidase II) that is overexpressed in prostate cancer.[12] PSMA PET scan is used for initial staging of high-risk prostate cancer and detecting its recurrences.

In assessing response to treatment of bone metastases, bone scan is recommended by guidelines of Prostate Cancer Working Group 3.[13] ^{18}F-NaF PET/CT has been reported to be an accurate imaging modality in the assessment of treatment response in patients with bone-only metastases from prostate cancer.[14] However, bone scan has certain limitations for assesing response to treatments because bone healing or flare response can cause increased uptake, which may cause difficulty at interpreting images.[15] Uptake due to flare phenomenon lasts approximately 6–12 months after chemotherapy. To avoid misinterpretation of the flare reaction, it is recommended to wait 6 months before evaluating the response to treatments or repeating the bone scan.[16] Due to long waiting time, radionuclide bone imaging is not useful in early response assessment to treatments. MRI was reported to be not affected by flare response and has a potential for early response assessment to treatments.[17] Role of PSMA PET scan in assesing response to treatments of bone metastases remains less clear. Androgen-axis targeted agents upregulate PSMA as a result of the interruption of androgen signaling, which may change the tracer uptake and the apparent extent of the disease.[18]

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

Corresponding author: Prof. Dr. Ismet Sarikaya, Department of Nuclear Medicine, Faculty of Medicine, Kirklareli University, Kırklareli, Turkey. isarikaya99@yahoo.com.

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Conflicts of interest

There are no conflicts of interest.

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